IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

UNITED STATES OF AMERICA, Plaintiff, v. BAYER CORPORATION, Defendant.	)	No. 2:07-cv-0001-JLL-JAD (Hon. Jose L. Linares)

BRIEF OF *AMICUS CURIAE* NATURAL PRODUCTS ASSOCIATION

Of Counsel:

Richard J. Oparil
Kevin M. Bell
PORZIO, BROMBERG
& NEWMAN P.C.
1200 New Hampshire Avenue, NW
Suite 710
Washington, DC 20036
Tel: 202.517.1888
Fax: 202.517.6322
roparil@pbnlaw.com
kmbell@pbnlaw.com

Alvin Weiss (AW7653)
PORZIO, BROMBERG
& NEWMAN P.C.
100 Southgate Parkway
P.O. Box 1997
Morristown, NJ 07962-1997
Tel: 973.538.4006
Fax: 973.538.5146
aweiss@pbnlaw.com

Counsel for Amicus Curiae
Natural Products Association

Dated: March 13, 2015

TABLE OF CONTENTS

TABLE OF AUTHORITIES

CASES

STATUTES

REGULATIONS

OTHER AUTHORITIES

INTEREST OF THE *AMICI*

Founded in 1936, the Natural Products Association ("NPA") is the nation's largest and oldest nonprofit organization dedicated to the natural products industry.[1] NPA advocates for the right of consumers to have access to products that will maintain and improve their health, and for the right of retailers and suppliers to sell these products. NPA represents over 1,900 members (94 of which are based in New Jersey), accounting for more than 10,000 retail, manufacturing, wholesale, and distribution locations of natural products, including foods, dietary supplements, and health/beauty aids. NPA unites a diverse membership, from the smallest health food store to the largest dietary supplement manufacturer. Defendant Bayer Corporation ("Bayer") is not an NPA member.

NPA played a key role in the passage of the Dietary Supplement Health and Education Act of 1994 ("DSHEA"), Pub. L. No. 103-417, 108 Stat. 4325. This important legislation struck a balance between the need for consumers to have access to and information about safe and effective dietary supplements while also preserving the government's interest in protecting the public from unsafe products and false and misleading claims. NPA's CEO and Executive Director, Daniel

[1] Natural products are represented by a wide array of consumer goods that grow in popularity each year. These products include natural and organic foods, dietary supplements, pet foods, health and beauty products, "green" cleaning supplies and more. Generally, natural products are considered those formulated without artificial ingredients and that are minimally processed.

Fabricant, Ph.D., previously served as the Director of Dietary Supplement Programs at the Food and Drug Administration.

INTRODUCTION

The Government seeks to hold Bayer in contempt regarding substantiation of its claims that its Phillips' Colon Health product ("PCH"), a probiotic supplement containing three bacteria types to help defend against occasional constipation, diarrhea, gas and bloating. The motion rests solely on the shoulders of one doctor, Loren Laine ("Laine"), who opines that the only way for Bayer to substantiate its PCH claims—or any structure/function claim—would be by conducting one or more drug-level randomized, controlled, double blind clinical trials ("RCTs") on the product.

What concerns NPA and its members is the opinion expressed by Laine that such RCTs would be required to substantiate structure/function claims of *all* human dietary supplements. The Government has not rejected that opinion; to the contrary, it is attempting to force that standard on the industry by picking off one company at a time through litigation and administrative proceedings. That strategy, however, is contrary to federal statute, the long-standing guidance documents of the Food and Drug Administration ("FDA") and Federal Trade Commission ("FTC"), and the First Amendment. If the Government wants to change the evidentiary requirements for substantiation of structure/function claims, it should

at least follow the Administrative Procedure Act and engage in notice and comment rulemaking.

While it takes no position on the ultimate disposition of the pending contempt motion as to Bayer, NPA and its members urge the Court to reject a broad requirement that structure/function claims for human dietary supplements may only be substantiated using the expensive and burdensome RCTs as designed by the Government's expert. A contrary result would devastate the dietary supplement industry and cause consumers to lose access to supplements that they want to use.

BACKGROUND

NPA will leave it to the parties to this litigation to provide the Court with a full discussion of the facts and the supporting evidence. For context, NPA notes that the case arose from a 2007 consent order that required Bayer to possess "competent and reliable scientific evidence" for dietary supplement claims. Dkt. No. 2 at 3-5. Bayer's product packaging and advertising states that PCH "Helps Defend Against Occasional: Constipation, Diarrhea, Gas and Bloating." Even though the standard for claim substantiation for dietary supplements is "competent and reliable scientific evidence," the Government argues that Bayer's structure/function claims must be substantiated by "gold standard" or drug-level

RCTs.[2] Because Bayer allegedly did not have such RCTs for PCH, the Government argues that Bayer did not substantiate its claims with competent and reliable evidence and it should be held in contempt.

The Government's motion rests wholly on the opinion of Laine, a medical doctor specializing in gastroenterology. He concedes that he is not an expert in dietary supplements or claim substantiation. *See, e.g.*, Dkt. No. 73-2 at 376:4-6. He has not conducted studies on dietary supplements. *See, e.g., id*. at 382:1-383:10. He rendered his opinions without either reading or being familiar in any way with the DSHEA statute or the relevant guidelines issued by the FDA and the FTC. *See, e.g., id*. at 182:16-183:19, 197:2-5, 217:1-14, 234:4-236:10. He testified that his opinions do not take the law or regulations into account. *See, e.g., id*. at 183:20-184:10, 194:15-195:8.[3] He testified that he has no understanding of what a

[2] *See* Dkt. No. 4-8 at 5 (the Government's study design "requires" RCTs that meet each and every one of these elements: "a randomized, placebo-controlled, double-blind trial of the products for which the claim is being made (e.g., PCH) in the population for which the claim is intended, using validated methods to access the outcome (e.g., symptoms of constipation, diarrhea, or gas and bloating), and using appropriate statistical methods to determine the sample size and analyze the results.").

[3] Laine did not even try to ensure that his opinion was consistent with applicable law:

> Q. So you did not undertake to ensure that your opinion is consistent with the statute [DSHEA], correct?
>
> A. Again, my opinion had nothing to do with any regulatory or legal issues. It was only based on the science and clinical research issues.

"structure/function" claim means. *See, e.g., id*. at 207:14-208:18, 209:8-21. Laine has never used the phrase "competent and reliable scientific evidence", which is the standard to be applied here. *Id*. at 402:17-404:10.

Shockingly, Laine states that the balance Congress struck in enacting the carefully considered dietary supplement regulatory regime is irrelevant and should simply be ignored. *See, e.g., id*. at 187:20-190:22 ("Congress [is] not known for their scientific expertise."), 192:4-12; 193:5-194:1, 194:15-196:21. Laine opines that the "**only way**" to substantiate claims for drugs **and** human dietary supplements is to conduct drug-level RCTs. *See, e.g., id*. at 54:16-56-12 (emphasis added), 132:3-10, 223:15-224:10, 229:11-21, 444:3-44519, 447:13-448:2. He testified that scientific evidence from animal, *in vitro*, or genetic studies could never be used to substantiate supplement claims and that only well-designed human RCTs would suffice. *Id*. at 238:5-17, 243:7-245:9, 246:16-249:18, 250:6-11. Moreover, he believes that the RCTs must be conducted using the specific formulation of the product being sold. *Id*. at 306:11-307:2. Laine also revealed that

---

> Q. You understand that this statute regulates dietary supplements in the United States, right?
>
> A. Nope.
>
> Q. You're aware that Congress made express findings on this, right?
>
> A. Nope.

Id. at 183:20-184:10.

his analysis did not consider the cost of doing RCTs to meet his testing criteria. *Id*. at 180:22-182:15.

The Government has not disavowed Laine's overbroad opinion in this case. While the Government's brief purports to limit Laine's opinion to the probiotic-supplement claims at issue, Laine himself disagrees. He unambiguously testified that, as a matter of science, his high-quality RCT study design would apply to probiotics *and* all other dietary supplements, as well as "foods" and all "other interventions":

> Q. In your scientific judgment, should the level of evidence, the standard of evidence to use their words vary between probiotic supplements and other dietary supplements?
>
> A. And what I was suggesting, as I said earlier, it would be the same regardless; supplement, food, or other interventions.

Id. at 445:13-19.

ARGUMENT

I. THE COMPETENT AND RELIABLE SCIENTIFIC EVIDENCE STANDARD FOR SUBSTANTIATING HUMAN DIETARY SUPPLEMENT CLAIMS DOES NOT REQUIRE THE USE OF DRUG-LEVEL RCTS AS DESIGNED BY THE GOVERNMENT'S EXPERT.

Simply put, Laine's opinion that a human dietary supplement claim can only be substantiated by the use of "gold standard" or drug-level RCTs is contrary to statutory law, administrative guidance, and case law. The Government is improperly trying to rewrite the law in a way that will unnecessarily burden the

supplement industry, cause safe and useful supplements to be pulled from store shelves and greatly increase costs to consumers. That is not what Congress intended when it unanimously passed DSHEA and President Clinton signed it into law.

A. The Government's Position Is Contrary To DSHEA.

Contrary to the Government's suggestion, DSHEA is highly relevant to this case. DSHEA passed in 1994 as a direct response to the Government's hostility to dietary supplements. As the Senate Committee on Labor and Human Resources reported: "Despite a voluminous scientific record indicating the potential health benefits of dietary supplements, the Food and Drug Administration has pursued a heavy-handed enforcement agenda against dietary supplements for over 30 years." Sen. Rep. No. 103-410 at 14 (103d Cong. 2d Sess.); *see also id.* at 17 (FDA's actions after enactment of the Nutrition Labeling and Education Act of 1990 ("NLEA"), Pub. L. No. 101-535, 104 Stat. 2353, "show the need for congressional action to assure citizens have continued access to dietary supplements and information about their benefits")[4]; 139 CONG. REC. S4577 (daily ed. Apr. 7, 1993)

[4] The FTC proposed implementing regulations that required use of a "significant scientific agreement" standard for supplements. Because of concerns that the NLEA would lead to dietary supplements being pulled from store shelves, Congress enacted the Dietary Supplement Act of 1992, Pub. L. No. 102-571, 106 Stat. 4500, which placed a temporary moratorium on the implementation of the NLEA as it applied to supplements.

(statement of Sen. Hatch) ("For more than three decades, FDA has tried to restrict severely the ability of the dietary supplement industry to sell and market its products and, consequently, the ability of consumers to buy them. The agency has repeatedly attempted to impose unnecessarily stringent standards that would leave many if not most supplement companies with no practical choice but to close their doors."); 140 CONG. REC. S14780 (daily ed. Oct. 7, 1994) (statement of Sen. Harkin) (DSHEA "guarantees the American people access to supplements to their diets that promote improved health and well-being. It also takes steps to assure that consumers will receive truth and nonmisleading information about these products without excessive, biassed regulation by the Federal government.").

Asserting that "improving the health status of United States citizens ranks at the top of the national priorities of the Federal Government" and that "the importance of nutrition and the benefits of dietary supplements to health promotion and disease prevention have been documented increasingly in scientific studies," DSHEA became law on October 25, 1994 and took effect in 1996.[5] The statute represented a victory for the millions of consumers of dietary supplements who felt

---

[5] DSHEA § 2. The statute defines a dietary supplement as: "a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following ingredients: (A) a vitamin; (B) a mineral; (C) an herb or other botanical; (D) an amino acid; (E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or (F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E)." 21 U.S.C. § 321(ff).

that the FDA advocated unreasonable regulatory guidelines. The language of the statute addressed this concern by stating that "the Federal Government should not take any actions to impose unreasonable regulatory barriers limiting or slowing the flow of safe products and accurate information to consumers" and that "dietary supplements are safe within a broad range of intake, and safety problems with the supplements are relatively rare." DSHEA § 2. DSHEA further found that "consumers should be empowered to make choices about preventive health care programs based on data from scientific studies of health benefits related to particular dietary supplements. *Id.* § 2(8).

Dietary supplement labels cannot claim to treat a disease, but may contain statements of nutritional support, in which "the statement claims a benefit related to a classical nutrient deficiency disease and discloses the prevalence of such disease in the United States, describes the role of a nutrient or dietary ingredient intended to *affect the structure or function in humans*, characterizes the documented mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function, or describes general well-being from consumption of a nutrient or dietary ingredient . . . ." 21 U.S.C. § 343(r)(6)(A) (emphasis added).[6]

[6] *See also* 21 C.F.R. § 101.93(f) ("Dietary supplement labels or labeling may, subject to the requirements in paragraphs (a) through (e) of this section, bear statements that describe the role of a nutrient or dietary ingredient intended to affect the structure or function in humans or that characterize the documented

Thus, structure/function claims describe the role of a dietary supplement in the structure and function of the human body but cannot claim to diagnose, mitigate, treat, cure, or prevent a disease. An example of a structure/function claim is the popular dietary supplement St. John's Wort, which may claim to be a "mood-brightener" but not a cure for depression, which is a specific disease. *See, e.g.*, J. Beisler, DIETARY SUPPLEMENTS AND THEIR DISCONTENTS: FDA REGULATION AND THE DIETARY SUPPLEMENT HEALTH AND EDUCATION ACT OF 1994, 31 Rutgers L.J. 511, 517 n.29 (2000). Another example is from the DSHEA Senate Report, which noted that a claim that a calcium supplement provides a nutrient needed for strong bones is "entirely appropriate" as a structure/function claim and "does not create drug status for such a product." Sen. Rept. 103-410 at 26. According to the FDA, the type of claims at issue in this case are permissible structure/function claims, not disease claims. *See* Regulations on Statements Made for Dietary Supplements

---

mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function, provided that such statements are not disease claims under paragraph (g) of this section. If the label or labeling of a product marketed as a dietary supplement bears a disease claim as defined in paragraph (g) of this section, the product will be subject to regulation as a drug unless the claim is an authorized health claim for which the product qualifies."). A disease claim " is damage to an organ, part, structure, or system of the body such that it does not function properly (e.g., cardiovascular disease), or a state of health leading to such dysfunctioning (e.g., hypertension); except that diseases resulting from essential nutrient deficiencies (e.g., scurvy, pellagra) are not included in this definition." *Id.* § 101.93(g).

Concerning the Effect of the Product on the Structure or Function of the Body, 65 Fed. Reg. 1000-01, 2000 WL 4559, at *1028-29 (2000); *id.* at *1026 ("occasional constipation" is a structure/function claim); *id.* at *1031 ("alleviates . . . gas and bloating" are structure/function claims); FDA, Guidance for Industry: Structure/Function Claims, Small Entity Compliance Guide (2002) (Criterion 8) (http://www.fda.gov/food/guidanceregulation/guidancedocumentsregulatoryinformation/ucm103340.htm). The Government does not and cannot dispute that the claims at issue are structure/function claims.

DSHEA requires that a statement of nutritional support (*i.e.*, a structure/function claim) must have "substantiation that such statement is truthful and not misleading" and contain a disclaimer that the "statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease." 21 U.S.C. § 343(r)(6)(B)-(C). Contrary to what the Government is arguing here, DSHEA was intended to counteract "unnecessarily stringent" federal intervention into the manufacturing, sale, labelling of dietary supplements and government overregulation. 139 CONG. REC. S4577 (daily ed. Apr. 7, 1993) (statement of Sen. Hatch); 139 CONG. REC. S17049 (daily ed. Nov. 23, 1993) (statement of Sen. Hatch). Consumer well-being is improved when there is greater access to dietary supplements. *Id*. Supplement producers should be free from intervention as long as "the labelling and advertising

are truthful, non-misleading, and there exists a reasonable scientific basis for products claims." *Id*. There isn't the slightest indication in the legislative history that a dietary supplement provider should conduct drug-level RCTs to substantiate the labelling of the products. To the contrary, dietary supplement providers only need to provide a reasonably scientific basis for the claims. *Id*. Thus, the Government's position in this case directly contradicts Congress's intent in passing DSHEA. And, as discussed above, Laine designed his RCTs test without any knowledge of DSHEA or the purpose behind it.

B. FTC And FDA Guidance Documents Do Not Require Drug-Level RCTs To Provide Competent And Reliable Scientific Evidence To Substantiate Structure/Function Claims.

Nor did Laine have any knowledge of or consider the administrative guidance that the supplement industry has operated under for years. The FDA recognized that "DSHEA's purpose [is] to broaden the scope of labeling claims that may be made for dietary supplements without subjecting them to regulation as drugs." 65 Fed. Reg. 1000-01, 2000 WL 4559 at *1024. Consistent with that purpose, substantiation of structure/function claims under DSHEA requires only that manufacturers have "competent and reliable scientific evidence," which has been defined to include "tests, analyses, research, studies, or other evidence . . . ." Guidance for Industry: Structure/Function Claims, Small Entity Compliance Guide (Criterion 8). Under DSHEA, dietary supplement manufacturers are not required to

conduct clinical trials or efficacy testing. *See* FDA Comment Request, Substantiation for Dietary Supplement Claims Made Under the Federal Food, Drug, and Cosmetic Act, 76 Fed. Reg. 51988-01, 2011 WL 3624830 (2011).

Consistent with DSHEA, the FTC recognized in 2001 that the competent and reliable scientific evidence standard is lower and more flexible than the standard applicable to drugs. In fact, the FTC explained that, unlike with drugs, "[t]here is no fixed formula for the number or type of studies required" to measure "the adequacy of the scientific support for a specific advertising claim" for a dietary supplement. FTC, Dietary Supplements: An Advertising Guide for Industry at 9 (available at https://www.ftc.gov/system/files/documents/plain-language/bus09-dietary-supplements-advertising-guide-industry.pdf). The guidance wrote:

> The FTC typically requires claims about the efficacy or safety of dietary supplements to be supported with competent and reliable scientific evidence, defined in FTC cases as tests, analyses, research, studies, or other evidence based on the expertise of professionals in the relevant area, that have been conducted and evaluated in an objective manner by persons qualified to do so, using procedures generally accepted in the profession to yield accurate and reliable results. This is the same standard the FTC applies to any industry making health-related claims. There is no fixed formula for the number or type of studies required or for more specific parameters like sample size and study duration. There are, however, a number of considerations to guide an advertiser in assessing the adequacy of the scientific support for a specific advertising claim. 1.

Id. As to the amount and type of evidence, the FTC explained that:

> When no specific claim about the level of support is made, the evidence needed depends on the nature of the claim. A guiding principle for determining the amount and type of evidence that will be sufficient is what experts in the relevant area of study would generally consider to be adequate. The FTC will consider all forms of competent and reliable scientific research when evaluating substantiation. As a general rule, well-controlled human clinical studies are the most reliable form of evidence. Results obtained in animal and in vitro studies will also be examined, particularly where they are widely considered to be acceptable substitutes for human research or where human research is infeasible. Although there is no requirement that a dietary supplement claim be supported by any specific number of studies, the replication of research results in an independently-conducted study adds to the weight of the evidence. In most situations, the quality of studies will be more important than quantity. When a clinical trial is not possible (e.g., in the case of a relationship between a nutrient and a condition that may take decades to develop), epidemiologic evidence may be an acceptable substitute for clinical data, especially when supported by other evidence, such as research explaining the biological mechanism underlying the claimed effect.

Id. at 10. By contrast, drug claims must be supported by "substantial evidence", which generally requires gold standard RCTs to show safety and efficacy. *See, e.g.*, 21 U.S.C. § 355(d); 21 C.F.R. § 314.126.

Thus, for 14 years, the industry has relied on the administrative guidance that the evidence needed to support a dietary supplement claim depends on many factors, including the type of product, the type of claim, the benefits of a truthful claim, the cost of developing substantiation, the consequences of a false claim, and the amount of substantiation that experts in the field believe is reasonable. While gold standard RCTs are the most reliable form of evidence, they are not necessarily

required; animal studies, in vitro studies, and epidemiological evidence will often suffice. As discussed above, the Government's expert, Laine, testified that he was unfamiliar with the guidance, but nevertheless believes that animal and *in vitro* studies can never be used to substantiate human dietary supplement claims.

C. Case Law Does Not Require Drug-Level/Gold Standard RCTs For All Human Dietary Supplement Claims.

The idea that human dietary supplement claims *must* be substantiated by "gold standard" RCTs of the type suggested by the Government and Laine has been rejected by several courts. For example, in *FTC v. QT, Inc.*, 512 F.3d 858 (7th Cir. 2008), the Court found that a claim could be substantiated without conducting a full clinical trial:

> Some passages in [the District Court decision] could be read to imply that any statement about a product's therapeutic effects must be deemed false unless the claim has been verified in a placebo-controlled, double blind study . . .
>
> Nothing in the Federal Trade Commission Act, the foundation of this litigation, requires placebo-controlled, double-blind studies. The Act forbids false and misleading statements, and a statement that is plausible but has not yet been tested in the most reliable way cannot be condemned out of hand. The burden is on the [government] to prove that the statements are false.… Think about the seller of an adhesive bandage treated with a disinfectant such as iodine. The seller does not need to conduct tests before asserting that this product reduces the risk of infection from cuts. The bandage keeps foreign materials out of the cuts and kills some bacteria. It may be debatable how much the risk of infection falls, but the direction of the effect would be known, and the claim could not be condemned as false. Placebo-controlled, double-blind testing is not a legal requirement for consumer products.

Id. at 862. Judge Easterbrook also noted that "[a] placebo-controlled study is the best test; something less may do (for there is no point in spending $1 million to verify a claim worth only $10,000 if true) ...." *Id.*

The decision in *Basic Research v. FTC*, Mem. Decision and Order, No. 2:09-cv-0779 (D. Utah Nov. 25, 2014) (submitted as Dkt. No. 73-7), is also instructive. There, the FTC contended that Basic Research violated a consent order (which required substantiation with "competent and reliable" scientific evidence) in advertising two weight loss supplement products. While Basic Research had supporting studies, they did not meet the "gold standard" test that the FTC's expert in that case said was required – a clinically significant finding in a randomized double-blind, placebo controlled, clinical study with the results published in a peer reviewed scientific journal. *Id*. at 7. The FTC argued that Basic Research's studies did not meet each of those elements and thus did not qualify as competent and reliable scientific evidence. *Id*. The District Court, however, rejected the FTC's argument, finding that "competent and reliable" scientific evidence does not require the "gold standard" but could be met by "various factors." *Id*. The Court ruled that:

> Although the Agreement states that "tests, analyses, research, studies, or other evidence" must use "procedures generally accepted in the profession to yield accurate and reliable results," the FTC has failed to show that the only procedures accepted in the profession are those that meet the ideal or the Gold Standard. Indeed, by characterizing a

> procedure as "ideal," it contemplates that other procedures may be adequate and accepted in the profession as well. Basic Research's experts confirm that while the Gold Standard may be ideal, it is not the only evidence accepted in the profession as yielding accurate and reliable results.

Id. at 22-23. The Court noted that substantiation evidence could include animal and *in vitro* studies and by drawing inferences and correlations between different studies. *Id*. at 25-26. Finally, the Court found that "[t]he FTC plays an important role of ensuring that advertising claims are adequately supported so that consumers may have confidence in a product. Implicit in that role, however, is the expectation of *reasonableness*. Here, the approach taken by the FTC through its expert requires a level of substantiation that exceeds the requirements" of the consent order. *Id*. at 26 (emphasis added).

In *FTC v. Garden of Life*, 845 F. Supp. 2d 1328, 1335 (S.D. Fla. 2012), *aff'd in part and vacated in part*, 516 F. App'x. 852 (11th Cir. 2013), the Court rejected the FTC's argument that a supplement manufacturer violated a consent order that required substantiation by "competent and reliable" scientific evidence. Garden of Life had hired an expert, who reviewed the available scientific evidence and concluded that the claims being made were substantiated. The FTC's expert disagreed with the design of the study, but the Court concluded that was not enough to grant the FTC's contempt motion. Accepting that argument, according to

the Court, would improperly read additional requirements into the consent order. *Id*. at 1334-35.

The First Circuit has held that even with respect to disease claims (*i.e.*, non-structure/function claims), full-blown RCTs may not be required. In *FTC v. Direct Mktg. Concepts, Inc*., 624 F.3d 1 (1st Cir. 2010), the FTC alleged that a supplement manufacturer did not have any scientific substantiation for claims that its products cured a variety of diseases. The Court declined to adopt the FTC's argument that the claims could only be substantiated by double-blind, placebo-controlled human studies. The Court ruled that "there may be other scientific evidence that could be sufficient, and we may assume for these purposes that a double-blind study is not necessarily required." *Id*. at 9.

Another disease claim case is the recent decision in *POM Wonderful, LLC v. FTC*, 2015 WL 394093 (D.C. Cir. Jan. 30, 2015). There, in an administrative proceeding, the FTC found POM violated the FTC Act by advertising that its pomegranate-based products could treat or prevent heart disease, prostate cancer and erectile dysfunction. The advertising allegedly mischaracterized the scientific evidence concerning the benefits of POM's products. The FTC found that one or more randomized and controlled human clinical trials were necessary to establish a causal relationship between those products and the treatment, prevention, or reduction of risk of heart disease, prostate cancer, or erectile dysfunction. *Id*. *11.

However, in reaching that conclusion, the FTC itself emphasized the distinction between "generalized nutritional and health benefit claims" and "the specific disease treatment and prevention claims at issue in this case," *i.e.*, "that the Challenged POM Products treat, prevent or reduce the risk of heart disease, prostate cancer, and ED, and that such claims are scientifically established." *Id*. at *12 (citation omitted). Even the FTC did not require randomized, controlled, human clinical trials to support non-disease claims. *Id*. at *7. Thus, the FTC itself recognized the distinction between the level of substantiation between structure/function and disease claims – a distinction that it is attempting to blur in this case.

It is also worth noting that in *Matrixx Initiatives, Inc. v. Siracusano*, 131 S.Ct. 1309 (2011), the Supreme Court found that neither medical practitioners nor the federal government "limit the data they consider to the results of randomized clinical trials or to statistically significant evidence." *Id*. at 1320 (quoting amicus brief of researchers). Indeed, the FDA does not require statistically significant RCTs before it bans the introduction of drugs based on suspected health risks. Id.

Thus, imposing full-scale clinical trials to substantiate structure/function nutritional statement claims does not find support in DSHEA, existing regulatory guidance or case law. As such, the Government's unreasonable attempt to do so in this case should be rejected.

D. Other Scientists Disagree With Dr. Laine's Opinion.

Finally, Dr. Laine's opinion that all human dietary supplement claims require substantiation by RCTs has been rebutted by Dr. Jeffrey Blumberg, who has a Ph.D. in pharmacology and currently is the Director of the Antioxidants Research Laboratory at Tufts University. Dkt. No. 73-6 at 2. He also teaches at Tufts' Friedman School of Nutrition Science and Policy and its Medical School. *Id*. at 3. Unlike Dr. Laine, Dr. Blumberg has published research on dietary supplements using RCTs as well as *in vitro* and animal studies. *Id*. at 2. Dr. Blumberg has opined that:

> The drug-level RCTs that Dr. Laine describes in his expert declaration are not required to show that a food or dietary ingredient has a health effect. In my expert opinion, "competent and reliable scientific evidence" for a structure/function claim can be obtained from the totality of several well-established research approaches, including in vitro experiments, animal models, population-based cohorts (observational research), and clinical trials, including but not limited to RCTs.

Id. at 5. He went on to aver that:

> It is clear from my experience that my scientific colleagues in the industry as well as colleagues in academia do not require or expect RCTs on dietary supplements. During my discussions regarding the development and substantiation of new products or reformulation of existing products to support a structure/function benefit, we always included the full range of available research results and research strategies. Consistent with the criteria established by Sir Austin Bradford Hill, we included other types of human clinical trials, observational studies, cohort studies, animal studies, and in vitro studies, to name a few. It was generally accepted that these studies could be sufficient to meet the FDA and FTC standard of competent

> and reliable scientific evidence. Many products are marketed on the basis of these studies, without robust RCT evidence.
>
> While RCTs were always considered when such studies existed, they were never treated as the only research approach through which relevant knowledge could be derived about nutrients and other dietary constituents. If Dr. Laine's drug-level RCT criteria became the law, it would effectively remove almost all of the existing dietary supplements with structure/function claims from the market. Moreover under this test, companies would be deterred from developing many other dietary supplements making structure/function claims.

Id. at 13.

Dr. Blumberg also criticized Dr. Laine's view that substantiation requires RCTs using the exact formulation for the product being sold. For example, he points out that he knows of no multivitamin supplement on the market that has been tested for structure/function claims in its combined form. Thus, "Dr. Laine's test would have far reaching implications if applied to structure/function statements regarding dietary supplements." *Id*. at 10; *see also* Expert Declaration of Dr. Daniel J. Merenstein, Dkt. No. 73-4 at 11 ("If Dr. Laine's tests were required for probiotics and supplements, it would likely require all supplement advertising to be eliminated, greatly impacting public health.").[7]

[7] The NIH Office of Dietary Supplements recommends that Americans consume Vitamin C, notwithstanding the lack of RCTs supporting disease prevention and health benefits. *See* NIH, Dietary Supplement Fact Sheet: Vitamin C (available at http://ods.od.nih.gov/factsheets/VitaminC-HealthProfessional/); Dkt. No. 73-4 at 11.

The broad opinion of the Government's expert that structure/function claims for human dietary supplements requires RCTs is belied by the sworn statement of Dr. Blumberg, an accomplished researcher in the supplement field. Dr. Laine's view is contradicted by the law, prior administrative guidance, cases and the scientific evidence. As such, the Court should not impose a requirement for RCTs on the dietary supplement industry.

II. THE GOVERNMENT IS IMPROPERLY TRYING TO USE CONSENT ORDERS AND CONTEMPT PROCEEDINGS TO REMAKE THE DIETARY SUPPLEMENT INDUSTRY.

While NPA and its members support the prevention of unfair and deceptive acts, they are concerned about the use of consent orders to impose requirements on the dietary supplement industry that exceed the scope of the law and past practices.[8] As the Government has admitted in this case, the consent order at issue contains a definition of "competent and reliable scientific evidence" that is "*identical*" to the definition that applies to the entire industry through the FTC's guidance. Dkt. No. 73-8, Resp. to Req. for Admission No. 1 (emphasis added).

[8] *See, e.g.*, *In the Matter of Nestle Health Care Nutrition, Inc.*, No. 0923087 (FTC May 18, 2010) (available at http://www.ftc.gov/sites/default/files/documents/cases/2010/07/100714nestleorder.pdf); *FTC v. Iovate Health Sciences USA, Inc.*, No. 10-cv-587 (W.D.N.Y. July 29, 2010) (available at http://www.ftc.gov/enforcement/cases-proceedings/072-3187/iovate-health-sciences-usa-inc).

The issue here is thus not limited to Bayer but applies to the entire supplement industry.

When application of extra-statutory interpretations moves from consent orders into rules of general applicability, such overreach is not beneficial to anyone, particularly consumers. One example would be the Government's view that additional studies and research are necessary prior to advertising, specifically, a requirement to conduct drug-level RCTs to support legal structure/function statements, which is not a current legal or regulatory requirement.

This is not only outside of the statute, but leads to unnecessary and inefficient use of resources, which chills innovation and disincentivizes the very research needed to substantiate claims. Laine's study design did not even consider any cost-benefit analysis on behalf of consumers or the economy, as he readily admitted. *See* Dkt. No. 73-2 at 180:22-182:15. Further, if the Court issues a broad ruling on the use of gold standard RCTs to support structure/function claims, it would send a message that companies would no longer be able to rely on the variety of studies conducted on their products. Moreover, gold standard RCTs for supplements are not always possible or ethical, and in many instances are cost prohibitive. Also relevant is that, unlike drug makers, supplement companies rarely own patents on their natural products that would grant them a period of exclusivity

to recoup their expense in conducting full-blown RCTs. *See* 35 U.S.C. § 101 (products of nature are not patentable).

The Government is attempting to eliminate the difference between structure/function and disease claims for dietary supplements using litigation-driven settlements with individual companies.[9] This strategy has caused confusion in the industry on how to comply with DSHEA and existing FDA and FTC guidance, increasing the risks to companies in the supplement market. As discussed above, overregulation of dietary supplements was the driving force behind passage of DSHEA in 1994. Despite that statute and the clear intent of Congress, the use of consent orders is moving the industry to a point where it appears the Government is equating structure/function nutritional statement claims with drug claims. If that happens, safe and effective supplements will disappear from store shelves, particularly products formulated, made and sold by small businesses that will simply be unable to afford the huge costs associated with the same kind of clinical trials required to bring drugs to market, *i.e.*, multiple gold

[9] Linda Goldstein, A New Paradigm in FTC Regulation, Inside Counsel (Feb. 27, 2013) (available at http://www.insidecounsel.com/2013/02/27/regulatory-a-new-paradigm-in-ftc-regulation) ("Although historically FTC case law, statutory provisions, trade regulation rules and guides provided the primary source of FTC jurisprudence, the agency is increasingly using consent order provisions to establish industry guidance and standards on a variety of advertising-related issues. Although technically these consent order provisions are binding only for the entities that sign them, they are often clearly designed to send a message to the entire industry regarding FTC expectations.").

standard RCTs.[10] The only possible alternative would be to avoid making otherwise scientifically-supported structure/function claims, which would have the constitutionally-suspect effect of deterring protected commercial speech and depriving consumers of useful information.

Assuming *arguendo* that the legal standard the Government wants could be obtained without repealing DSHEA, at the very least the Government should implement the change through proper procedures, including notice and comment rulemaking under the Administrative Procedure Act, Pub. L. 79–404, 60 Stat. 237. That process would permit the supplement industry, consumers and other stakeholders to participate in a full analysis and discussion of the costs and benefits of changes to the regulatory scheme. The *ad hoc* nature of regulatory changes using consent orders – and contempt proceedings – improperly limits the discussion to only the litigants (and any *amici*) and excludes the public. It would also enable NPA's members to know with some certainty what the standard is that they must meet. The current approach where DSHEA and agency guidance says one thing, and the Government in litigation documents takes the opposite position,

[10] *See QT Inc.*, 515 F.3d at 861 (requiring costly RCTs could subject "vendors to bear such heavy costs [and] may keep useful products off the market … and prevent vendors from making truthful statements that will help consumers locate products that will do them good.").

is disruptive and counterproductive as it chills protected speech and limits consumers access to safe and effective supplements.

III. A REQUIREMENT THAT STRUCTURE/FUNCTION REQUIRE GOLD STANDARD RCTS WOULD IMPLICATE FIRST AMENDMENT RIGHTS.

It is well-established that commercial speech is protected by the First Amendment. *See, e.g.*, *Va. State Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc.*, 425 U.S. 748, 770 (1976). This protection has "great relevance" in "the fields of medicine and public health." *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653, 2664 (2011). Any regulation limiting such claims can be upheld only if (1) "the asserted governmental interest is substantial"; (2) "the regulation directly advances the governmental interest asserted"; and (3) "it is not more extensive than is necessary to serve that interest." *Central Hudson Gas & Elec. Corp. v. Public Serv. Comm'n*, 447 U.S. 557, 566 (1980); *see also Sorrell*, 131 S. Ct. at 2659 ("Speech in aid of pharmaceutical marketing ... is a form of expression protected by the . . . First Amendment" and striking down a statute that burdened such speech).

To be sure, false or misleading speech is not protected. *See, e.g.*, *Va. State Bd. of Pharmacy*, 425 U.S. at 771; *POM Wonderful*, 2015 WL 394093, *18; 15 U.S.C. § 45(a)(1) (FTC Act prohibits deceptive practices); 15 U.S.C. § 1125 (Lanham Act). However, any restriction on commercial speech must be no broader

than reasonably necessary to prevent deception. *See, e.g.*, *FTC v. Brown & Williamson Tobacco Corp.*, 778 F.2d 35, 43 (D.C. Cir. 1985). The Government cannot ban speech unless it is first proved to be true to a scientific certainty. *See Pearson v. Shalala*, 164 F.3d 650, 655 (D.C. Cir. 1999) (lack of "significant scientific agreement" about health claims made by dietary supplement manufacturers does not allow the government to ban that speech as false or misleading). And, as discussed above, the *POM Wonderful* decision held that requiring two RCTs for disease claims was contrary to the First Amendment:

> Here, the consequences of mandating more than one RCT bear emphasis. Requiring additional RCTs without adequate justification exacts considerable costs, and not just in terms of the substantial resources often necessary to design and conduct a properly randomized and controlled human clinical trial. If there is a categorical bar against claims about the disease-related benefits of a food product or dietary supplement in the absence of two RCTs, consumers may be denied useful, truthful information about products with a demonstrated capacity to treat or prevent serious disease. That would subvert rather than promote the objectives of the commercial speech doctrine.

2015 WL 394093, *21.

Congress, in enacting DSHEA, deliberately distinguished dietary supplements from drugs so that claims in support of supplements – which it viewed as generally safe and useful products – would be subject to a more lenient standard. *See* DSHEA § 2. There is no “substantial” government interest in countermanding Congress’s mandate by holding dietary supplements making general

structure/function claims to the same standard as drugs or disease claims. Nor, can the government plausibly contend that requiring drug-like RCT proof for dietary supplement structure/function claims "is not more extensive than is necessary" to achieve any legitimate purpose of protecting against fraud. *Pearson*, 164 F.3d at 656-58. The government's position in this case conflicts with the First Amendment. Thus, the Court should construe the law to avoid the constitutional issue. *See Edward J. DeBartolo Corp. v. Fla. Gulf Coast Bldg. & Constr. Trades Council*, 485 U.S. 568, 575 (1988).

CONCLUSION

NPA and its members have serious concerns about the attempt of the Government and its expert to rewrite federal law and impose costly drug-like clinical trial requirements on safe and beneficial dietary supplements with structure/function claims. The drug-level RCTs standard the Government is attempting to impose on all supplements for humans is inconsistent with law and administrative guidance. NPA also opposes the Government's efforts to remake the supplement industry and restrict commercial speech protected by the First Amendment through litigation over consent orders that do not expressly require RCTs and without engaging in notice-and-comment rulemaking that would allow all stakeholders to be heard. NPA respectfully requests that the Court not make a

broad ruling that would decimate the dietary supplement industry and restrict consumer choice.

Dated: March 11, 2015

Respectfully submitted,

/s/ Alvin Weiss

Alvin Weiss (AW7653)
PORZIO, BROMBERG
& NEWMAN P.C.
100 Southgate Parkway
P.O. Box 1997
Morristown, NJ 07962-1997
Tel: 973.538.4006
Fax: 973.538.5146
aweiss@pbnlaw.com

Counsel for Amicus Curiae
Natural Products Association

Of Counsel:

Richard J. Oparil
Kevin M. Bell
PORZIO, BROMBERG
& NEWMAN P.C.
1200 New Hampshire Avenue, NW
Suite 710
Washington, DC 20036
Tel: 202.517.1888
Fax: 202.517.6322
roparil@pbnlaw.com
kmbell@pbnlaw.com

CERTIFICATE OF SERVICE

The undersigned hereby certifies that the foregoing was served on counsel for all parties through the Court's ECF system on March 13, 2015.

/s/ Alvin Weiss
Alvin Weiss (AW7653)